APPLN. FILING DATE: MAY 26, 2000
TITLE: REGULATING LIPID LEVELS VIA THE ZMAX1
OR H GENE
INVENTOR(S): JOHN P. CARULLI ET AL.
APPLICATION SERIAL NO: 09/578,900







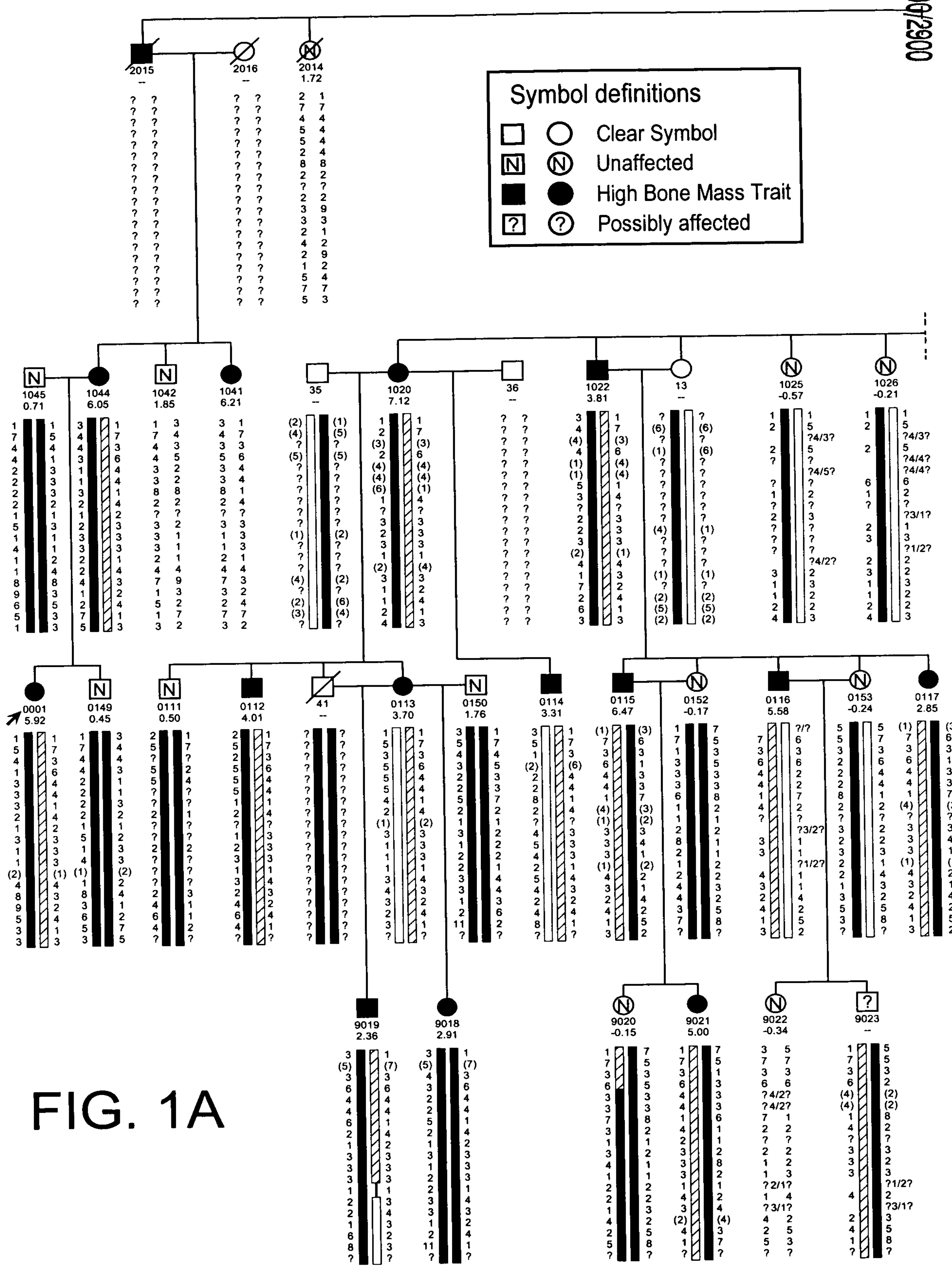



FIG. 1A

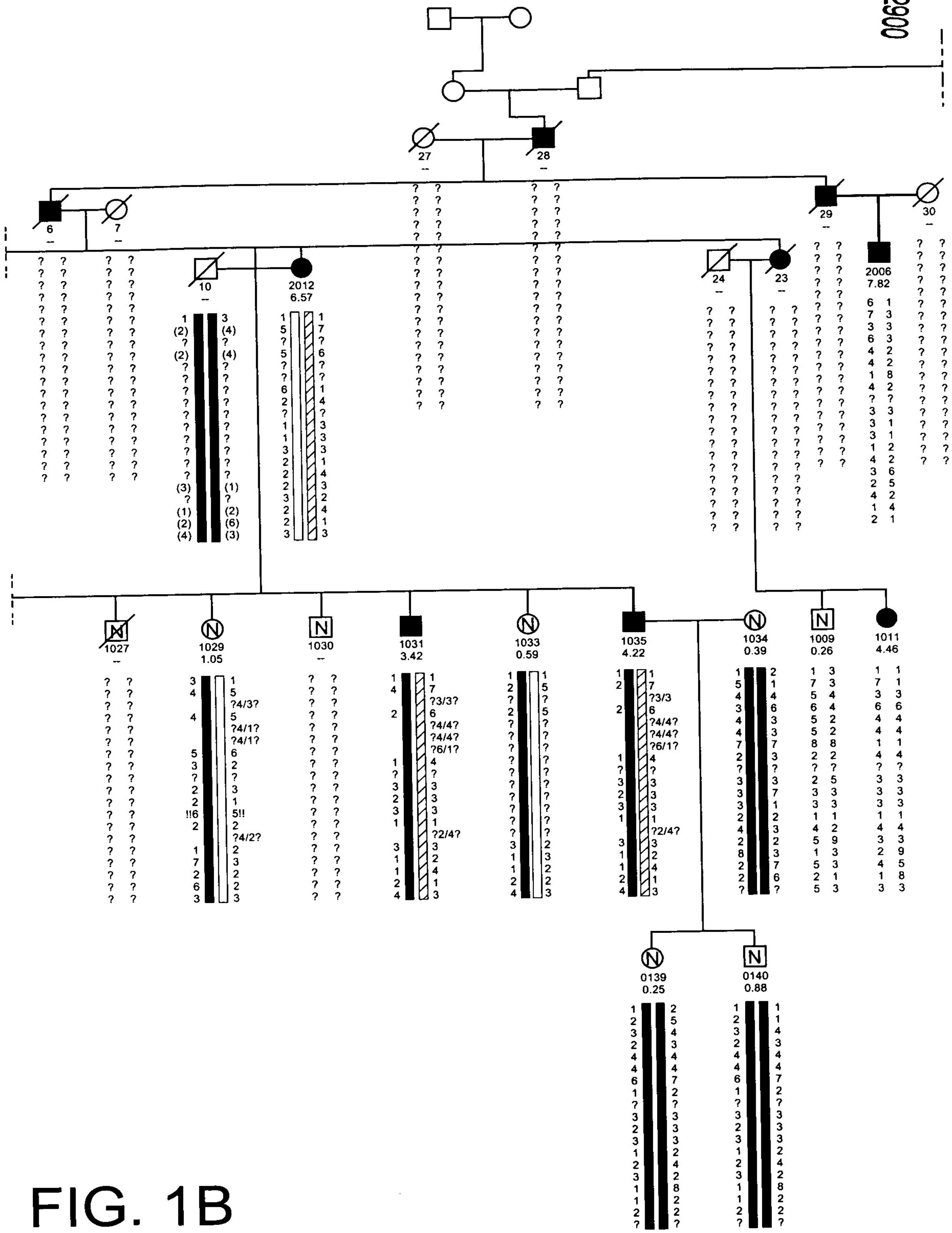

27
28
6
7
29
30
10
2012
6.57
24
23
2006
7.82
1027
1029
1.05
1030
1031
3.42
1033
0.59
1035
4.22
1034
0.39
1009
0.26
1011
4.46
0139
0.25
0140
0.88

FIG. 1B

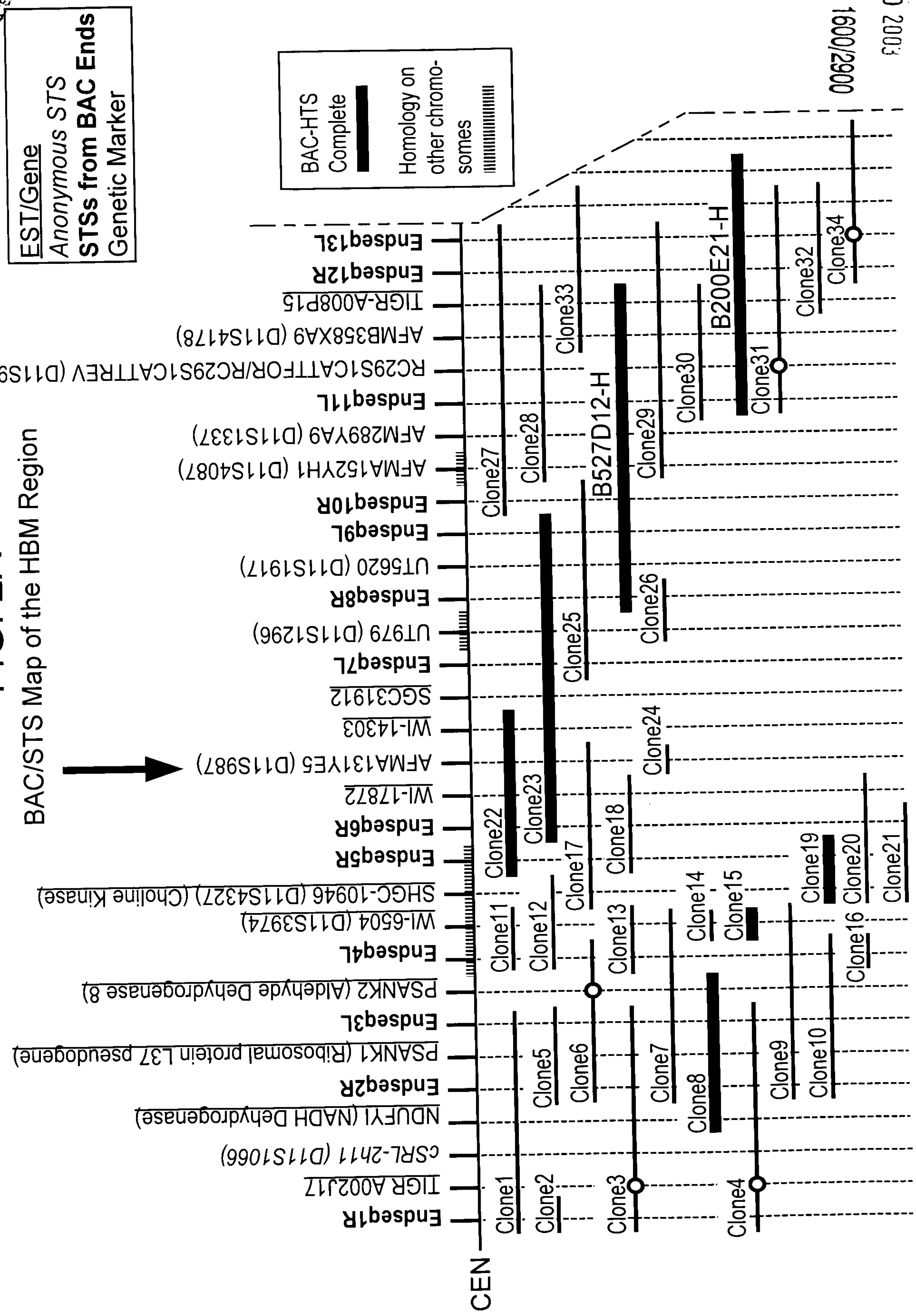



FIG. 2A
BAC/STS Map of the HBM Region

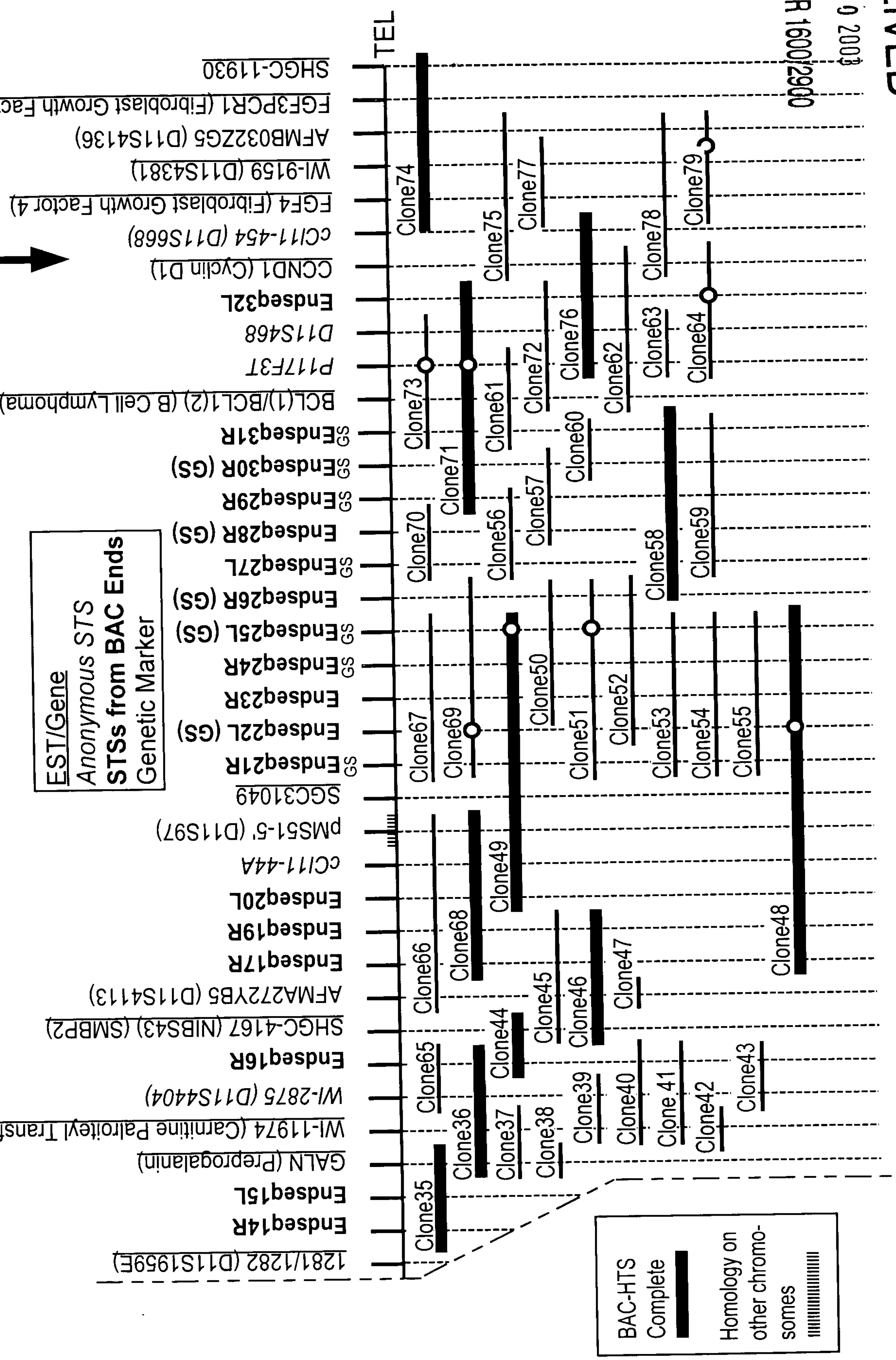



FIG. 2B
BAC/STS Map of the HBM Region

**Exon 1**
ACTAAAGCGCCGCCGCCGCGCCATGGAGCCCGAGTGAGCGCGGCGCG
GGCCCGTCCGGCCGCCGGACAACATGGAGGCAGCGCCGCCCGGGCCG
CCGTGGCCGCTGCTGCTGCTGCTGCTGCTGCTGCTGGCGCTGTGCGGC
TGCCCGGCCCCCGCCGCGGCC

**Exon 2 Coordinates: 527d12_Contig308G 30944-30549**
gccccacagCCTCGCCGCTCCTGCTATTTGCCAACCGCCGGGACGTACGGC
TGGTGGACGCCGGCGGAGTCAAGCTGGAGTCCACCATCGTGGTCAGC
GGCCTGGAGGATGCGGCCGCAGTGGACTTCCAGTTTTCCAAGGGAGC
CGTGTACTGGACAGACGTGAGCGAGGAGGCCATCAAGCAGACCTACCT
GAACCAGACGGGGGCCGCCGTGCAGAACGTGGTCATCTCCGGCCTGG
TCTCTCCCGACGGCCTCGCCTGCGACTGGGTGGGCAAGAAGCTGTACT
GGACGGACTCAGAGACCAACCGCATCGAGGTGGCCAACCTCAATGGC
ACATCCCGGAAGGTGCTCTTCTGGCAGGACCTTGACCAGCCGAGGGCC
ATCGCCTTGGACCCCGCTCACGGgtaaaccctgctg

... 9408 nt ...

**Exon 3 Coordinates: 527d12_Contig308G 21141-20945**
ccccgtcacagGTACATGTACTGGACAGACTGGGGTGAGACGCCCCGGATTG
AGCGGGCAGGGATGGATGGCAGCACCCGGAAGATCATTGTGGACTCG
GACATTTACTGGCCCAATGGACTGACCATCGACCTGGAGGAGCAGAAG
CTCTACTGGGCTGACGCCAAGCTCAGCTTCATCCACCGTGCCAACCTG
GACGGCTCGTTCCGgtaggtacccac

... 6094 nt ...

**Exon 4 Coordinates: 527d12_Contig308G 15047-14850**
tccctgactgcagGCAGAAGGTGGTGGAGGGCAGCCTGACGCACCCCTTCGCC
CTGACGCTCTCCGGGGACACTCTGTACTGGACAGACTGGCAGACCCGC
TCCATCCATGCCTGCAACAAGCGCACTGGGGGGAAGAGGAAGGAGAT
CCTGAGTGCCCTATACTCACCCATGGACATCCAGGTGCTGAGCCAGGA
GCGGCAGCCTTTCTgtgagtgccgg

... 1827 nt ...

**Exon 5 Coordinates: 527d12_Contig308G 13220-13088**
tttctcagTCCACACTCGCTGTGAGGAGGACAATGGCGGCTGCTCCCACCTG
TGCCTGCTGTCCCCAAGCGAGCCTTTCTACACATGCGCCTGCCCCACG
GGTGTGCAGCTGCAGGACAACGGCAGGACGTGTAAGGCAGgtgaggcggtgg
gacg

**FIG. 3A**

... 20923 nt ...

**Exon 6 Coordinates: 527d12_Contig309G 7705-8100**
ctccacag**GAGCCGAGGAGGTGCTGCTGCTGGCCCGGCGGACGGACCTAC
GGAGGATCTCGCTGGACACGCCGGACTTCACCGACATCGTGCTGCAGG
TGGACGACATCCGGCACGCCATTGCCATCGACTACGACCCGCTAGAGG
GCTATGTCTACTGGACAGATGACGAGGTGCGGGCCATCCGCAGGGCG
TACCTGGACGGGTCTGGGGCGCAGACGCTGGTCAACACCGAGATCAA
CGACCCCGATGGCATCGCGGTCGACTGGGTGGCCCGAAACCTCTACTG
GACCGACACGGGCACGGACCGCATCGAGGTGACGCGCCTCAACGGCA
CCTCCCGCAAGATCCTGGTGTCGGAGGACCTGGACGAGCCCCGAGCC
ATCGCACTGCACCCCGTGATGGG**gtaagacgggc

….. 3211 nt …..

**Exon 7 Coordinates: 527d12_Contig309G 11311-11482**
ttcttctccag**CCTCATGTACTGGACAGACTGGGGAGAGAACCCTAAAATCGA
GTGTGCCAACTTGGATGGGCAGGAGCGGCGTGTGCTGGTCAATGCCTC
CCTCGGGTGGCCCAACGGCCTGGCCCTGGACCTGCAGGAGGGGAAGC
TCTACTGGGGAGACGCCAAGACAGACAAGATCGAG**gtgaggctcctgtgg

…… 13445 nt …..

**Exon 8 Coordinates: 527d12_Contig309G 24927-25143**
ccgtcctgcag**GTGATCAATGTTGATGGGACGAAGAGGCGGACCCTCCTGGA
GGACAAGCTCCCGCACATTTTCGGGTTCACGCTGCTGGGGGACTTCAT
CTACTGGACTGACTGGCAGCGCCGCAGCATCGAGCGGGTGCACAAGG
TCAAGGCCAGCCGGGACGTCATCATTGACCAGCTGCCCGACCTGATGG
GGCTCAAAGCTGTGAATGTGGCCAAGGTCGTCG**gtgagtccggggggtc

….2826 nt ……

**Exon 9 Coordinates: 527d12_Contig309G 27969-28256**
gttcgcttccag**GAACCAACCCGTGTGCGGACAGGAACGGGGGGTGCAGCCA
CCTGTGCTTCTTCACACCCCACGCAACCCGGTGTGGCTGCCCCATCGG
CCTGGAGCTGCTGAGTGACATGAAGACCTGCATCGTGCCTGAGGCCTT
CTTGGTCTTCACCAGCAGAGCCGCCATCCACAGGATCTCCCTCGAGAC
CAATAACAACGACGTGGCCATCCCGCTCACGGGCGTCAAGGAGGCCTC
AGCCCTGGACTTTGATGTGTCCAACAACCACATCTACTGGACAGACGT
CAGCCTGAAG**gtagcgtgggc

……3102…..

**FIG. 3B**

**Exon 10 Coordinates: 527d12_Contig309G 31358-31582**
cctgctgccag**ACCATCAGCCGCGCCTTCATGAACGGAGCTCGGTGGAGCA
CGTGGTGGAGTTTGGCCTTGACTACCCCGAGGGCATGGCCGTTGACTG
GATGGGCAAGAACCTCTACTGGGCCGACACTGGGACCAACAGAATCGA
AGTGGCGCGGCTGGACGGGCAGTTCCGGCAAGTCCTCGTGTGGAGGG
ACTTGGACAACCCGAGGTCGCTGGCCCTGGATCCCACCAAGGG**gtaagtgtt
tgcctgtc

......1297 nt......

**Exon 11 Coordinates: 527d12_Contig309G 32879-33064**
gtgccttccag**CTACATCTACTGGACCGAGTGGGGCGGCAAGCCGAGGATCG
TGCGGGCCTTCATGGACGGGACCAACTGCATGACGCTGGTGGACAAG
GTGGGCCGGGCCAACGACCTCACCATTGACTACGCTGACCAGCGCCTC
TACTGGACCGACCTGGACACCAACATGATCGAGTCGTCCAACATGCTG
G**gtgagggccgggct

.......2069 nt.....

**Exon 12 Coordinates: 527d12_Contig309G 35133-35454**
gtgttcatgcag**GTCAGGAGCGGGTCGTGATTGCCGACGATCTCCCGCACCCG
TTCGGTCTGACGCAGTACAGCGATTATATCTACTGGACAGACTGGAAT
CTGCACAGCATTGAGCGGGCCGACAAGACTAGCGGCCGGAACCGCAC
CCTCATCCAGGGCCACCTGGACTTCGTGATGGACATCCTGGTGTTCCA
CTCCTCCCGCCAGGATGGCCTCAATGACTGTATGCACAACAACGGGCA
GTGTGGGCAGCTGTGCCTTGCCATCCCCGGCGGCCACCGCTGCGGCT
GCGCCTCACACTACACCCTGGACCCCAGCAGCCGCAACTGCAGCC**gtaag
tgcctcatggt

.......2006 nt......

**Exon 13 Coordinates: 527d12_Contig309G 37460-37659**
gcctcctcta**CGCCCACCACCTTCTTGCTGTTCAGCCAGAAATCTGCCATCAG
TCGGATGATCCCGGACGACCAGCACAGCCCGGATCTCATCCTGCCCCT
GCATGGACTGAGGAACGTCAAAGCCATCGACTATGACCCACTGGACAA
GTTCATCTACTGGGTGGATGGGCGCCAGAACATCAAGCGAGCCAAGGA
CGACGGGACCCAG**gcaggtgccctgtgg

......6965 nt......

**FIG. 3C**

**Exon 14 Coordinates: 527d12_Contig309G 44624-44832**
ctttgtcttacagCCCTTTGTTTTGACCTCTCTGAGCCAAGGCCAAAACCCAGAC
AGGCAGCCCCACGACCTCAGCATCGACATCTACAGCCGGACACTGTTC
TGGACGTGCGAGGCCACCAATACCATCAACGTCCACAGGCTGAGCGG
GGAAGCCATGGGGGTGGTGCTGCGTGGGGACCGCGACAAGCCCAGGG
CCATCGTCGTCAACGCGGAGCGAGGgtaggaggccaac

......1404 nt.....

**Exon 15 Coordinates: 527d12_Contig309G 46236-46427**
ccaccctcccgcagGTACCTGTACTTCACCAACATGCAGGACCGGGCAGCCAA
GATCGAACGCGCAGCCCTGGACGGCACCGAGCGCGAGGTCCTCTTCA
CCACCGGCCTCATCCGCCCTGTGGCCCTGGTGGTGGACAACACACTGG
GCAAGCTGTTCTGGGTGGACGCGGACCTGAAGCGCATTGAGAGCTGT
GACCTGTCAGgtacgcgccccgg

.....686 nt.....

**Exon 16 Coordinates: 527d12_Contig309G 47113-47322**
ggctgcttgcagGGGCCAACCGCCTGACCCTGGAGGACGCCAACATCGTGCA
GCCTCTGGGCCTGACCATCCTTGGCAAGCATCTCTACTGGATCGACCG
CCAGCAGCAGATGATCGAGCGTGTGGAGAAGACCACCGGGGACAAGC
GGACTCGCATCCAGGGCCGTGTCGCCCACCTCACTGGCATCCATGCAG
TGGAGGAAGTCAGCCTGGAGGAGTTCTgtacgtgggggc

.....3884 nt......

**Exon 17 Coordinates: 527d12_Contig309G 51206-51331**
ttgtctttgcagCAGCCCACCCATGTGCCCGTGACAATGGTGGCTGCTCCCACA
TCTGTATTGCCAAGGGTGATGGGACACCACGGTGCTCATGCCCAGTCC
ACCTCGTGCTCCTGCAGAACCTGCTGACCTGTGGAGgtaggtgtgacctaggtgc

....3905 nt.......

**Exon 18 Coordinates: 527d12_Contig309G 55236-55472**
gttctcctctgtccctcccccagAGCCGCCCACCTGCTCCCCGGACCAGTTTGCATGT
GCCACAGGGGAGATCGACTGTATCCCCGGGGCCTGGCGCTGTGACGG
CTTTCCCGAGTGCGATGACCAGAGCGACGAGGAGGGCTGCCCCGTGT
GCTCCGCCGCCCAGTTCCCCTGCGCGCGGGGTCAGTGTGTGGACCTGC
GCCTGCGCTGCGACGGCGAGGCAGACTGTCAGGACCGCTCAGACGAG
GTGGACTGTGACGgtgaggccctcc

.......3052 nt.....

**FIG. 3D**

**Exon 19 Coordinates: 527d12_Contig309G 58524-58634**
tctccttgcag**CCATCTGCCTGCCCAACCAGTTCCGGTGTGCGAGCGGCCAGT GTGTCCTCATCAAACAGCAGTGCGACTCCTTCCCCGACTGTATCGACG GCTCCGACGAGCTCATGTGTG**gtgagccagctt

........1448 nt......

**Exon 20 Coordinates: 527d12_Contig309G 60082-60319**
gtttgtctctggcag**AAATCACCAAGCCGCCCTCAGACGACAGCCCGGCCCACA GCAGTGCCATCGGGCCCGTCATTGGCATCATCCTCTCTCTCTTCGTCAT GGGTGGTGTCTATTTTGTGTGCCAGCGCGTGGTGTGCCAGCGCTATGC GGGGGCCAACGGGCCCTTCCCGCACGAGTATGTCAGCGGGACCCCGC ACGTGCCCCTCAATTTCATAGCCCCGGGCGGTTCCCAGCATGGCCCCT TCACAG**gtaaggagcctgagatatggaa

....1095 nt.....

**Exon 21 Coordinates: 527d12_Contig309G 61414-61552**
cttccctgccag**GCATCGCATGCGGAAAGTCCATGATGAGCTCCGTGAGCCTG ATGGGGGGCCGGGGCGGGGTGCCCCTCTACGACCGGAACCACGTCAC AGGGGCCTCGTCCAGCAGCTCGTCCAGCACGAAGGCCACGCTGTACCC GCCG**gtgaggggcggg

......6513 nt......

**Exon 22 Coordinates: 527d12_Contig309G 68065-68162**
ttggctctcctcag**ATCCTGAACCCGCCGCCCTCCCCGGCCACGGACCCCTCCC TGTACAACATGGACATGTTCTACTCTTCAAACATTCCGGCCACTGCGA GACCGTACAG**gtaggacatcccctgcag

.......2273 nt.....

**FIG. 3E**

**Exon 23 Coordinates: 527d12_Contig309G 70435-70901**

tcaaacattccggccactgcgagaccgtacag**GCCCTACATCATTCGAGGAATGGCGCCCC
CGACGACGCCCTGCAGCACCGACGTGTGACAGCGACTACAGCGCC
AGCCGCTGGAAGGCCAGCAAGTACTACCTGGATTTGAACTCGGACTCA
GACCCCTATCCACCCCCACCCACGCCCCACAGCCAGTACCTGTCGGCG
GAGGACAGCTGCCCGCCCTCGCCCGCCACCGAGAGGAGCTACTTCCAT
CTCTTCCCGCCCCCTCCGTCCCCCTGCACGGACTCATCC**TGACCTCGGC
CGGGCCACTCTGGCTTCTCTGTGCCCCTGTAAATAGTTTTAAATATGAACAA
AGAAAAAAATATATTTTATGATTTAAAAAATAAATATAATTGGGATTTTAA
AAACATGAGAAATGTGAACTGTGATGGGGTGGCAGGGCTGGGAGAACTT
TGTACAGTGGAGAAATATTTATAAACTTAATTTTGTAAAACA

**FIG. 3F**

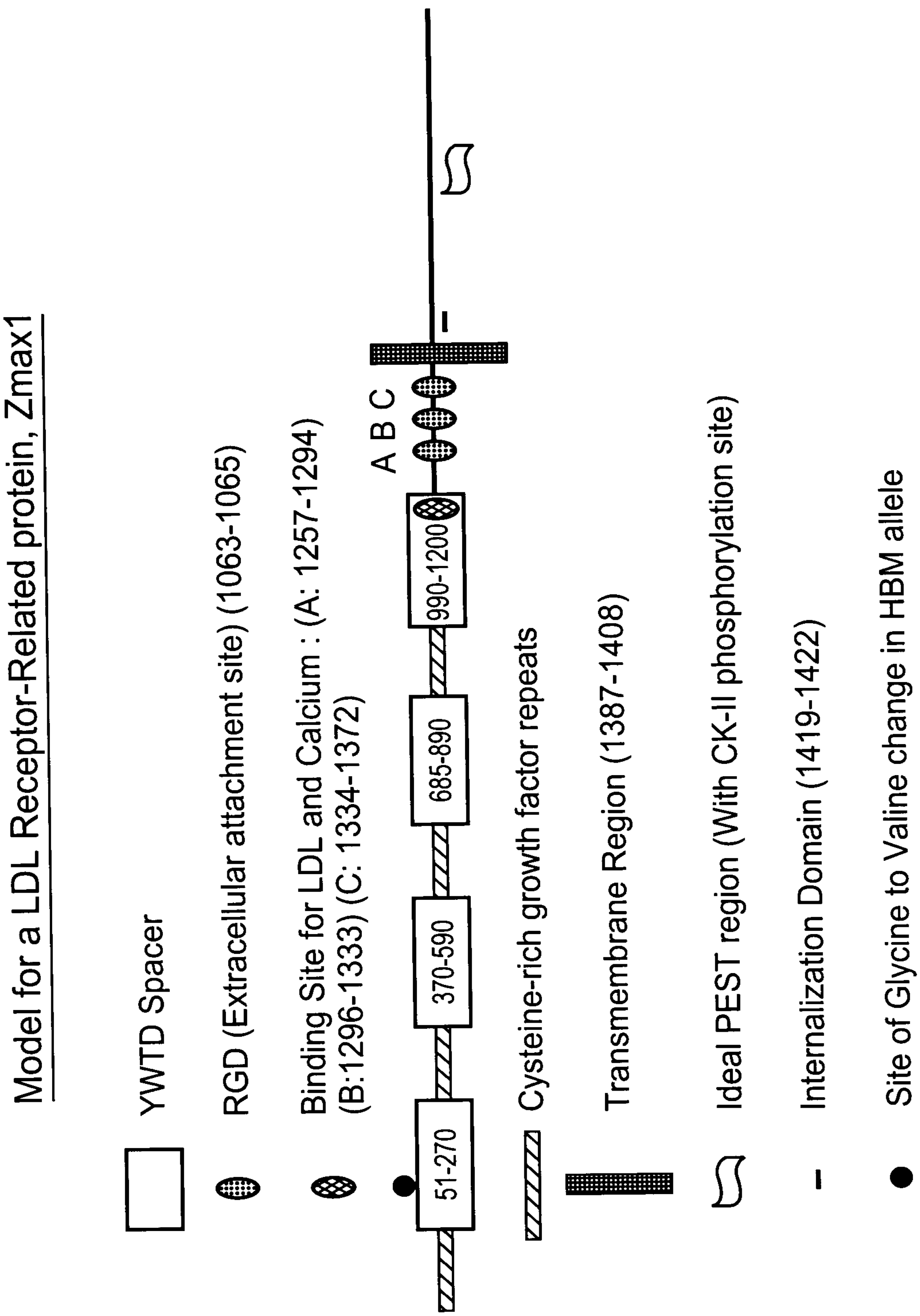
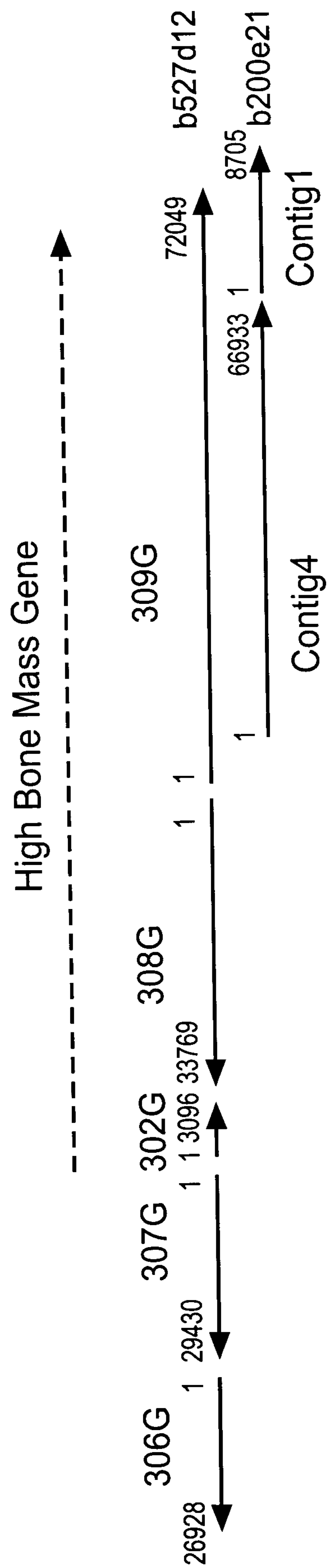

Model for a LDL Receptor-Related protein, Zmax1
YWTD Spacer
RGD (Extracellular attachment site) (1063-1065)
Binding Site for LDL and Calcium : (A: 1257-1294) (B:1296-1333) (C: 1334-1372)
Cysteine-rich growth factor repeats
Transmembrane Region (1387-1408)
Ideal PEST region (With CK-II phosphorylation site)
Internalization Domain (1419-1422)
Site of Glycine to Valine change in HBM allele
51-270
370-590
685-890
990-1200
A B C

FIG. 4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b200e21
8705
72049
Contig1
1
66933
Contig4
1
309G
High Bone Mass Gene
1
1
308G
33769
3096
1
1
302G
307G
29430
1
306G
26928

FIG. 5

# FIG. 6A

```
  1  ACTAAAGCGCCGCCGCCGCGCCATGGAGCCCGAGTGAGCGCGGCGCGGCCCGTCCGGCC   60
 61  GCCGGACAACATGGAGGCAGCGCCGCCCGGGCCGCCGTGGCCGCTGCTGCTGCTGCTGCT  120
  1                  M  E  A  A  P  P  G  P  P  W  P  L  L  L  L  L  L   17

121  GCTGCTGCTGGCGCTGTGCGGCTGCCCGGCCCCCGCCGCGGCCTCGCCGCTCCTGCTATT  180
 18   L  L  L  A  L  C  G  C  P  A  P  A  A  A  S  P  L  L  L  F   37

181  TGCCAACCGCCGGGACGTACGGCTGGTGGACGCCGGCGGAGTCAAGCTGGAGTCCACCAT  240
 38   A  N  R  R  D  V  R  L  V  D  A  G  G  V  K  L  E  S  T  I   57

241  CGTGGTCAGCGGCCTGGAGGATGCGGCCGCAGTGGACTTCCAGTTTTCCAAGGGAGCCGT  300
 58   V  V  S  G  L  E  D  A  A  A  V  D  F  Q  F  S  K  G  A  V   77

301  GTACTGGACAGACGTGAGCGAGGAGGCCATCAAGCAGACCTACCTGAACCAGACGGGGGC  360
 78   Y  W  T  D  V  S  E  E  A  I  K  Q  T  Y  L  N  Q  T  G  A   97

361  CGCCGTGCAGAACGTGGTCATCTCCGGCCTGGTCTCTCCCGACGGCCTCGCCTGCGACTG  420
 98   A  V  Q  N  V  V  I  S  G  L  V  S  P  D  G  L  A  C  D  W  117

421  GGTGGGCAAGAAGCTGTACTGGACGGACTCAGAGACCAACCGCATCGAGGTGGCCAACCT  480
118   V  G  K  K  L  Y  W  T  D  S  E  T  N  R  I  E  V  A  N  L  137

481  CAATGGCACATCCCGGAAGGTGCTCTTCTGGCAGGACCTTGACCAGCCGAGGGCCATCGC  540
138   N  G  T  S  R  K  V  L  F  W  Q  D  L  D  Q  P  R  A  I  A  157

541  CTTGGACCCCGCTCACGGGTACATGTACTGGACAGACTGGGGTGAGACGCCCCGGATTGA  600
158   L  D  P  A  H  G  Y  M  Y  W  T  D  W  G  E  T  P  R  I  E  177
```

# FIG. 6B

```
601   GCGGGCAGGGATGGATGGCAGCACCCGGAAGATCATTGTGGACTCGGACATTTACTGGCC   660
178    R  A  G  M  D  G  S  T  R  K  I  I  V  D  S  D  I  Y  W  P    197

661   CAATGGACTGACCATCGACCTGGAGGAGCAGAAGCTCTACTGGGCTGACGCCAAGCTCAG   720
198    N  G  L  T  I  D  L  E  E  Q  K  L  Y  W  A  D  A  K  L  S    217

721   CTTCATCCACCGTGCCAACCTGGACGGCTCGTTCCGGCAGAAGGTGGTGGAGGGCAGCCT   780
218    F  I  H  R  A  N  L  D  G  S  F  R  Q  K  V  V  E  G  S  L    237

781   GACGCACCCCTTCGCCCTGACGCTCTCCGGGGACACTCTGTACTGGACAGACTGGCAGAC   840
238    T  H  P  F  A  L  T  L  S  G  D  T  L  Y  W  T  D  W  Q  T    257

841   CCGCTCCATCCATGCCTGCAACAAGCGCACTGGGGGGAAGAGGAAGGAGATCCTGAGTGC   900
258    R  S  I  H  A  C  N  K  R  T  G  G  K  R  K  E  I  L  S  A    277

901   CCTCTACTCACCCATGGACATCCAGGTGCTGAGCCAGGAGCGGCAGCCTTTCTTCCACAC   960
278    L  Y  S  P  M  D  I  Q  V  L  S  Q  E  R  Q  P  F  F  H  T    297

961   TCGCTGTGAGGAGGACAATGGCGGCTGCTCCCACCTGTGCCTGCTGTCCCCAAGCGAGCC   1020
298    R  C  E  E  D  N  G  G  C  S  H  L  C  L  L  S  P  S  E  P    317

1021  TTTCTACACATGCGCCTGCCCCACGGGTGTGCAGCTGCAGGACAACGGCAGGACGTGTAA   1080
318    F  Y  T  C  A  C  P  T  G  V  Q  L  Q  D  N  G  R  T  C  K    337

1081  GGCAGGAGCCGAGGAGGTGCTGCTGCTGGCCCGGCGGACGGACCTACGGAGGATCTCGCT   1140
338    A  G  A  E  E  V  L  L  L  A  R  R  T  D  L  R  R  I  S  L    357
```

# FIG. 6C

```
1141  GGACACGCCGGACTTCACCGACATCGTGCTGCAGGTGGACGACATCCGGCACGCCATTGC  1200
358    D  T  P  D  F  T  D  I  V  L  Q  V  D  D  I  R  H  A  I  A   377

1201  CATCGACTACGACCCGCTAGAGGGCTATGTCTACTGGACAGATGACGAGGTGCGGGCCAT  1260
378    I  D  Y  D  P  L  E  G  Y  V  Y  W  T  D  D  E  V  R  A  I   397

1261  CCGCAGGGCGTACCTGGACGGGTCTGGGGCGCAGACGCTGGTCAACACCGAGATCAACGA  1320
398    R  R  A  Y  L  D  G  S  G  A  Q  T  L  V  N  T  E  I  N  D   417

1321  CCCCGATGGCATCGCGGTCGACTGGGTGGCCCGAAACCTCTACTGGACCGACACGGGCAC  1380
418    P  D  G  I  A  V  D  W  V  A  R  N  L  Y  W  T  D  T  G  T   437

1381  GGACCGCATCGAGGTGACGCGCCTCAACGGCACCTCCCGCAAGATCCTGGTGTCGGAGGA  1440
438    D  R  I  E  V  T  R  L  N  G  T  S  R  K  I  L  V  S  E  D   457

1441  CCTGGACGAGCCCCGAGCCATCGCACTGCACCCCGTGATGGGCCTCATGTACTGGACAGA  1500
458    L  D  E  P  R  A  I  A  L  H  P  V  M  G  L  M  Y  W  T  D   477

1501  CTGGGGAGAGAACCCTAAAATCGAGTGTGCCAACTTGGATGGGCAGGAGCGGCGTGTGCT  1560
478    W  G  E  N  P  K  I  E  C  A  N  L  D  G  Q  E  R  R  V  L   497

1561  GGTCAATGCCTCCCTCGGGTGGCCCAACGGCCTGGCCCTGGACCTGCAGGAGGGGAAGCT  1620
498    V  N  A  S  L  G  W  P  N  G  L  A  L  D  L  Q  E  G  K  L   517

1621  CTACTGGGGAGACGCCAAGACAGACAAGATCGAGGTGATCAATGTTGATGGGACGAAGAG  1680
518    Y  W  G  D  A  K  T  D  K  I  E  V  I  N  V  D  G  T  K  R   537
```

# FIG. 6D

1681 GCGGACCCTCCTGGAGGACAAGCTCCCGCACATTTTCGGGTTCACGCTGCTGGGGGACTT 1740
538 R T L L E D K L P H I F G F T L L G D F 557

1741 CATCTACTGGACTGACTGGCAGCGCCGCAGCATCGAGCGGGTGCACAAGGTCAAGGCCAG 1800
558 I Y W T D W Q R R S I E R V H K V K A S 577

1801 CCGGGACGTCATCATTGACCAGCTGCCCGACCTGATGGGGCTCAAAGCTGTGAATGTGGC 1860
578 R D V I I D Q L P D L M G L K A V N V A 597

1861 CAAGGTCGTCGGAACCAACCCGTGTGCGGACAGGAACGGGGGGTGCAGCCACCTGTGCTT 1920
598 K V V G T N P C A D R N G G C S H L C F 617

1921 CTTCACACCCCACGCAACCCGGTGTGGCTGCCCCATCGGCCTGGAGCTGCTGAGTGACAT 1980
618 F T P H A T R C G C P I G L E L L S D M 637

1981 GAAGACCTGCATCGTGCCTGAGGCCTTCTTGGTCTTCACCAGCAGAGCCGCCATCCACAG 2040
638 K T C I V P E A F L V F T S R A A I H R 657

2041 GATCTCCCTCGAGACCAATAACAACGACGTGGCCATCCCGCTCACGGGCGTCAAGGAGGC 2100
658 I S L E T N N N D V A I P L T G V K E A 677

2101 CTCAGCCCTGGACTTTGATGTGTCCAACAACCACATCTACTGGACAGACGTCAGCCTGAA 2160
678 S A L D F D V S N N H I Y W T D V S L K 697

2161 GACCATCAGCCGCGCCTTCATGAACGGGAGCTCGGTGGAGCACGTGGTGGAGTTTGGCCT 2220
698 T I S R A F M N G S S V E H V V E F G L 717

# FIG. 6E

```
2221  TGACTACCCCGAGGGCATGGCCGTTGACTGGATGGGCAAGAACCTCTACTGGGCCGACAC  2280
718    D  Y  P  E  G  M  A  V  D  W  M  G  K  N  L  Y  W  A  D  T   737

2281  TGGGACCAACAGAATCGAAGTGGCGCGGCTGGACGGGCAGTTCCGGCAAGTCCTCGTGTG  2340
738    G  T  N  R  I  E  V  A  R  L  D  G  Q  F  R  Q  V  L  V  W   757

2341  GAGGGACTTGGACAACCCGAGGTCGCTGGCCCTGGATCCCACCAAGGGCTACATCTACTG  2400
758    R  D  L  D  N  P  R  S  L  A  L  D  P  T  K  G  Y  I  Y  W   777

2401  GACCGAGTGGGGCGGCAAGCCGAGGATCGTGCGGGCCTTCATGGACGGGACCAACTGCAT  2460
778    T  E  W  G  G  K  P  R  I  V  R  A  F  M  D  G  T  N  C  M   797

2461  GACGCTGGTGGACAAGGTGGGCCGGGCCAACGACCTCACCATTGACTACGCTGACCAGCG  2520
798    T  L  V  D  K  V  G  R  A  N  D  L  T  I  D  Y  A  D  Q  R   817

2521  CCTCTACTGGACCGACCTGGACACCAACATGATCGAGTCGTCCAACATGCTGGGTCAGGA  2580
818    L  Y  W  T  D  L  D  T  N  M  I  E  S  S  N  M  L  G  Q  E   837

2581  GCGGGTCGTGATTGCCGACGATCTCCCGCACCCGTTCGGTCTGACGCAGTACAGCGATTA  2640
838    R  V  V  I  A  D  D  L  P  H  P  F  G  L  T  Q  Y  S  D  Y   857

2641  TATCTACTGGACAGACTGGAATCTGCACAGCATTGAGCGGGCCGACAAGACTAGCGGCCG  2700
858    I  Y  W  T  D  W  N  L  H  S  I  E  R  A  D  K  T  S  G  R   877

2701  GAACCGCACCCTCATCCAGGGCCACCTGGACTTCGTGATGGACATCCTGGTGTTCCACTC  2760
878    N  R  T  L  I  Q  G  H  L  D  F  V  M  D  I  L  V  F  H  S   897
```

# FIG. 6F

```
2761  CTCCCGCCAGGATGGCCTCAATGACTGTATGCACAACAACGGGCAGTGTGGGCAGCTGTG  2820
898    S  R  Q  D  G  L  N  D  C  M  H  N  N  G  Q  C  G  Q  L  C   917

2821  CCTTGCCATCCCCGGCGGCCACCGCTGCGGCTGCGCCTCACACTACACCCTGGACCCCAG  2880
918    L  A  I  P  G  G  H  R  C  G  C  A  S  H  Y  T  L  D  P  S   937

2881  CAGCCGCAACTGCAGCCCGCCCACCACCTTCTTGCTGTTCAGCCAGAAATCTGCCATCAG  2940
938    S  R  N  C  S  P  P  T  T  F  L  L  F  S  Q  K  S  A  I  S   957

2941  TCGGATGATCCCGGACGACCAGCACAGCCCGGATCTCATCCTGCCCCTGCATGGACTGAG  3000
958    R  M  I  P  D  D  Q  H  S  P  D  L  I  L  P  L  H  G  L  R   977

3001  GAACGTCAAAGCCATCGACTATGACCCACTGGACAAGTTCATCTACTGGGTGGATGGGCG  3060
978    N  V  K  A  I  D  Y  D  P  L  D  K  F  I  Y  W  V  D  G  R   997

3061  CCAGAACATCAAGCGAGCCAAGGACGACGGGACCCAGCCCTTTGTTTTGACCTCTCTGAG  3120
998    Q  N  I  K  R  A  K  D  D  G  T  Q  P  F  V  L  T  S  L  S  1017

3121  CCAAGGCCAAAACCCAGACAGGCAGCCCCACGACCTCAGCATCGACATCTACAGCCGGAC  3180
1018   Q  G  Q  N  P  D  R  Q  P  H  D  L  S  I  D  I  Y  S  R  T  1037

3181  ACTGTTCTGGACGTGCGAGGCCACCAATACCATCAACGTCCACAGGCTGAGCGGGGAAGC  3240
1038   L  F  W  T  C  E  A  T  N  T  I  N  V  H  R  L  S  G  E  A  1057

3241  CATGGGGGTGGTGCTGCGTGGGGACCGCGACAAGCCCAGGGCCATCGTCGTCAACGCGGA  3300
1058   M  G  V  V  L  R  G  D  R  D  K  P  R  A  I  V  V  N  A  E  1077
```

# FIG. 6G

```
3301  GCGAGGGTACCTGTACTTCACCAACATGCAGGACCGGGCAGCCAAGATCGAACGCGCAGC  3360
1078   R  G  Y  L  Y  F  T  N  M  Q  D  R  A  A  K  I  E  R  A  A   1097

3361  CCTGGACGGCACCGAGCGCGAGGTCCTCTTCACCACCGGCCTCATCCGCCCTGTGGCCCT  3420
1098   L  D  G  T  E  R  E  V  L  F  T  T  G  L  I  R  P  V  A  L   1117

3421  GGTGGTGGACAACACACTGGGCAAGCTGTTCTGGGTGGACGCGGACCTGAAGCGCATTGA  3480
1118   V  V  D  N  T  L  G  K  L  F  W  V  D  A  D  L  K  R  I  E   1137

3481  GAGCTGTGACCTGTCAGGGGCCAACCGCCTGACCCTGGAGGACGCCAACATCGTGCAGCC  3540
1138   S  C  D  L  S  G  A  N  R  L  T  L  E  D  A  N  I  V  Q  P   1157

3541  TCTGGGCCTGACCATCCTTGGCAAGCATCTCTACTGGATCGACCGCCAGCAGCAGATGAT  3600
1158   L  G  L  T  I  L  G  K  H  L  Y  W  I  D  R  Q  Q  Q  M  I   1177

3601  CGAGCGTGTGGAGAAGACCACCGGGGACAAGCGGACTCGCATCCAGGGCCGTGTCGCCCA  3660
1178   E  R  V  E  K  T  T  G  D  K  R  T  R  I  Q  G  R  V  A  H   1197

3661  CCTCACTGGCATCCATGCAGTGGAGGAAGTCAGCCTGGAGGAGTTCTCAGCCCACCCATG  3720
1198   L  T  G  I  H  A  V  E  E  V  S  L  E  E  F  S  A  H  P  C   1217

3721  TGCCCGTGACAATGGTGGCTGCTCCCACATCTGTATTGCCAAGGGTGATGGGACACCACG  3780
1218   A  R  D  N  G  G  C  S  H  I  C  I  A  K  G  D  G  T  P  R   1237

3781  GTGCTCATGCCCAGTCCACCTCGTGCTCCTGCAGAACCTGCTGACCTGTGGAGAGCCGCC  3840
1238   C  S  C  P  V  H  L  V  L  L  Q  N  L  L  T  C  G  E  P  P   1257
```

# FIG. 6H

3841 CACCTGCTCCCCGGACCAGTTTGCATGTGCCACAGGGGAGATCGACTGTATCCCCGGGGC 3900
1258 T C S P D Q F A C A T G E I D C I P G A 1277

3901 CTGGCGCTGTGACGGCTTTCCCGAGTGCGATGACCAGAGCGACGAGGAGGGCTGCCCCGT 3960
1278 W R C D G F P E C D D Q S D E E G C P V 1297

3961 GTGCTCCGCCGCCCAGTTCCCCTGCGCGCGGGGTCAGTGTGTGGACCTGCGCCTGCGCTG 4020
1298 C S A A Q F P C A R G Q C V D L R L R C 1317

4021 CGACGGCGAGGCAGACTGTCAGGACCGCTCAGACGAGGTGGACTGTGACGCCATCTGCCT 4080
1318 D G E A D C Q D R S D E V D C D A I C L 1337

4081 GCCCAACCAGTTCCGGTGTGCGAGCGGCCAGTGTGTCCTCATCAAACAGCAGTGCGACTC 4140
1338 P N Q F R C A S G Q C V L I K Q Q C D S 1357

4141 CTTCCCCGACTGTATCGACGGCTCCGACGAGCTCATGTGTGAAATCACCAAGCCGCCCTC 4200
1358 F P D C I D G S D E L M C E I T K P P S 1377

4201 AGACGACAGCCCGGCCCACAGCAGTGCCATCGGGCCCGTCATTGGCATCATCCTCTCTCT 4260
1378 D D S P A H S S A I G P V I G I I L S L 1397

4261 CTTCGTCATGGGTGGTGTCTATTTTGTGTGCCAGCGCGTGGTGTGCCAGCGCTATGCGGG 4320
1398 F V M G G V Y F V C Q R V V C Q R Y A G 1417

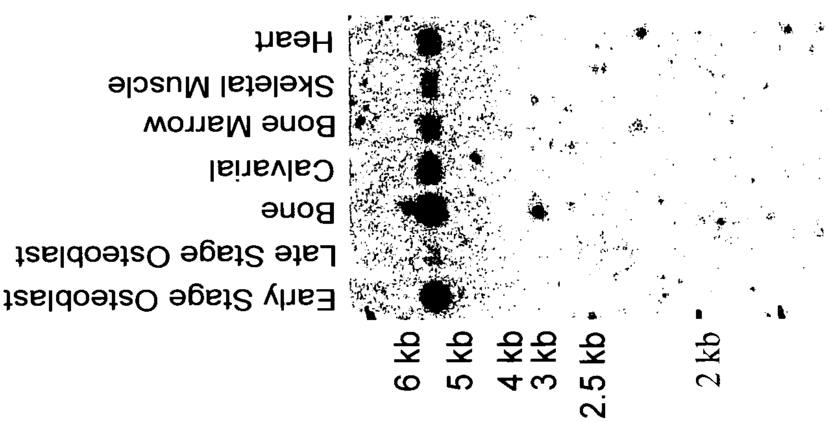
4321 GGCCAACGGGCCCTTCCCGCACGAGTATGTCAGCGGGACCCCGCACGTGCCCCTCAATTT 4380
1418 A N G P F P H E Y V S G T P H V P L N F 1437

# FIG. 6I

```
4381 CATAGCCCCGGGCGGTTCCCAGCATGGCCCCTTCACAGGCATCGCATGCGGAAAGTCCAT 4440
1438  I  A  P  G  G  S  Q  H  G  P  F  T  G  I  A  C  G  K  S  M  1457

4441 GATGAGCTCCGTGAGCCTGATGGGGGGCCGGGGCGGGGTGCCCCTCTACGACCGGAACCA 4500
1458  M  S  S  V  S  L  M  G  G  R  G  G  V  P  L  Y  D  R  N  H  1477

4501 CGTCACAGGGGCCTCGTCCAGCAGCTCGTCCAGCACGAAGGCCACGCTGTACCCGCCGAT 4560
1478  V  T  G  A  S  S  S  S  S  S  S  T  K  A  T  L  Y  P  P  I  1497

4561 CCTGAACCCGCCGCCCTCCCCGGCCACGGACCCCTCCCTGTACAACATGGACATGTTCTA 4620
1498  L  N  P  P  P  S  P  A  T  D  P  S  L  Y  N  M  D  M  F  Y  1517

4621 CTCTTCAAACATTCCGGCCACTGCGAGACCGTACAGGCCCTACATCATTCGAGGAATGGC 4680
1518  S  S  N  I  P  A  T  A  R  P  Y  R  P  Y  I  I  R  G  M  A  1537

4681 GCCCCCGACGACGCCCTGCAGCACCGACGTGTGTGACAGCGACTACAGCGCCAGCCGCTG 4740
1538  P  P  T  T  P  C  S  T  D  V  C  D  S  D  Y  S  A  S  R  W  1557

4741 GAAGGCCAGCAAGTACTACCTGGATTTGAACTCGGACTCAGACCCCTATCCACCCCCACC 4800
1558  K  A  S  K  Y  Y  L  D  L  N  S  D  S  D  P  Y  P  P  P  P  1577

4801 CACGCCCCACAGCCAGTACCTGTCGGCGGAGGACAGCTGCCCGCCCTCGCCCGCCACCGA 4860
1578  T  P  H  S  Q  Y  L  S  A  E  D  S  C  P  P  S  P  A  T  E  1597

4861 GAGGAGCTACTTCCATCTCTTCCCGCCCCCTCCGTCCCCCTGCACGGACTCATCCTGACC 4920
1598  R  S  Y  F  H  L  F  P  P  P  P  S  P  C  T  D  S  S        1615
```

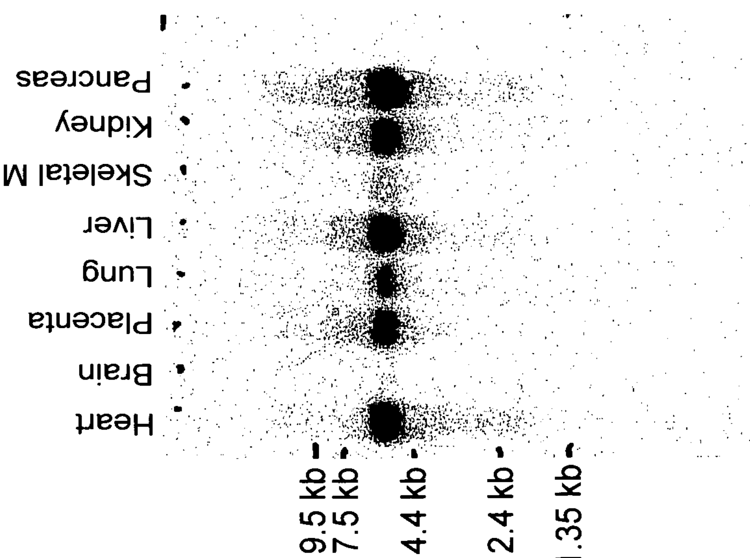
# FIG. 6J

```
4921  TCGGCCGGGCCACTCTGGCTTCTCTGTGCCCCTGTAAATAGTTTTAAATATGAACAAAGA  4980
4981  AAAAAATATATTTTATGATTTAAAAAATAAATATAATTGGGATTTTAAAAACATGAGAAA  5040
5041  TGTGAACTGTGATGGGGTGGGCAGGCTGGGAGAACTTTGTACAGTGGAGAAATATTTAT  5100
5101  AAACTTAATTTTGTAAAACA  5120
```




Northern Blot Analysis - Zmax 1

FIG. 7B




Northern Blot Analysis - Zmax 1

FIG. 7A

Zmax 1 random samples

b527d12-h_Contig087C_1.nt

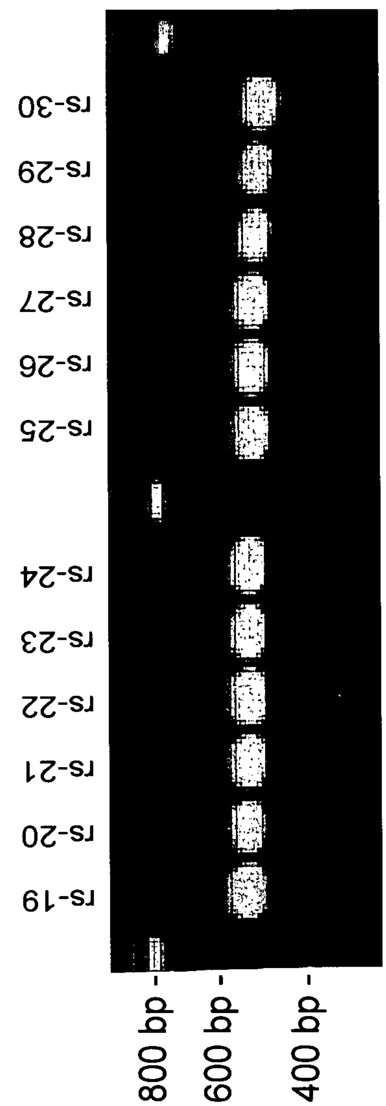



FIG. 8

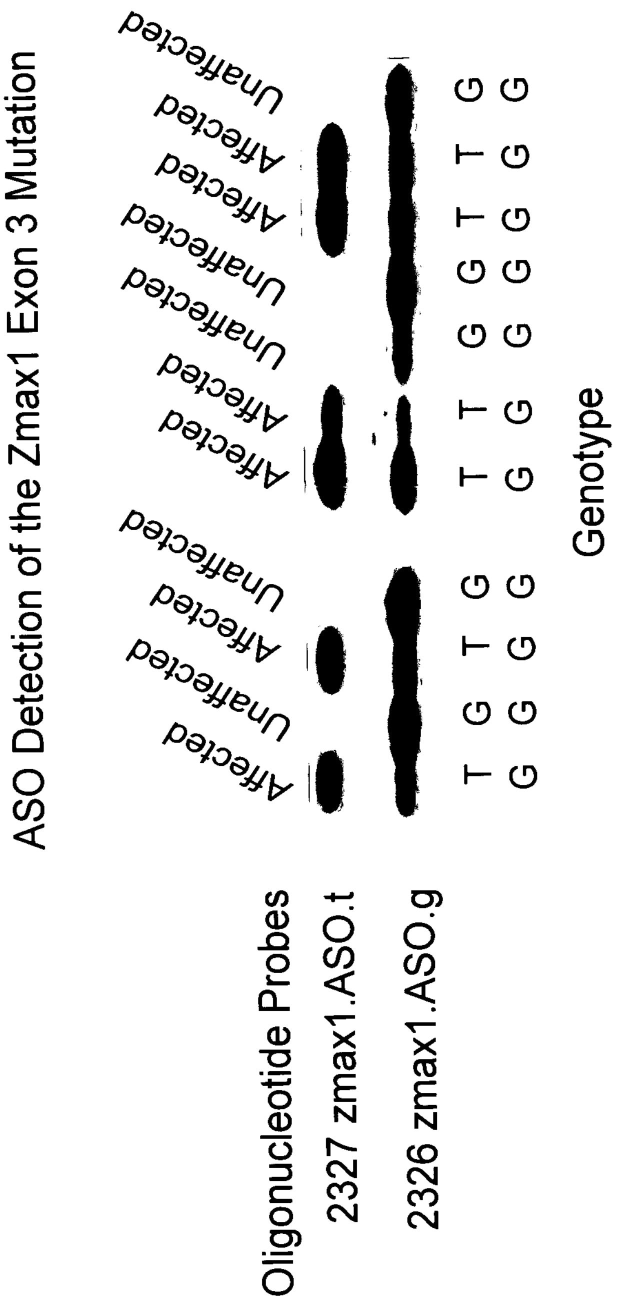

ASO Detection of the Zmax1 Exon 3 Mutation
Affected
Unaffected
Affected
Unaffected
Affected
Affected
Unaffected
Unaffected
Affected
Affected
Unaffected
Oligonucleotide Probes
2327 zmax1.ASO.t
2326 zmax1.ASO.g
T G T G T T G G T T G
G G G G G G G G G G G
Genotype

FIG. 9

Mouse Zmax1 In situ hybridization
100X Magnification

Antisense probe


FIG. 10A

Mouse Zmax1 In situ hybridization
100X Magnification

Sense probe

FIG. 10B

Mouse Zmax1 In situ hybridization
400X Magnification
Antisense probe

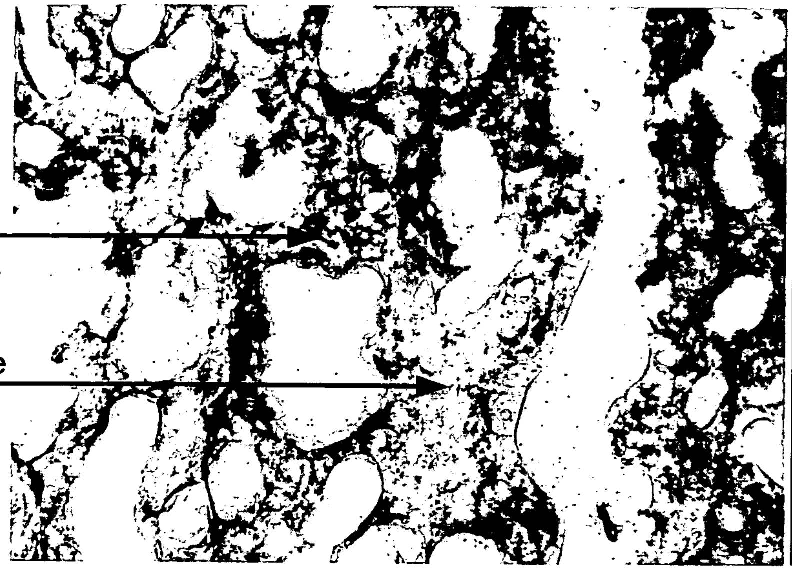



FIG. 11A

Mouse Zmax1 In situ hybridization
400X Magnification
Sense probe

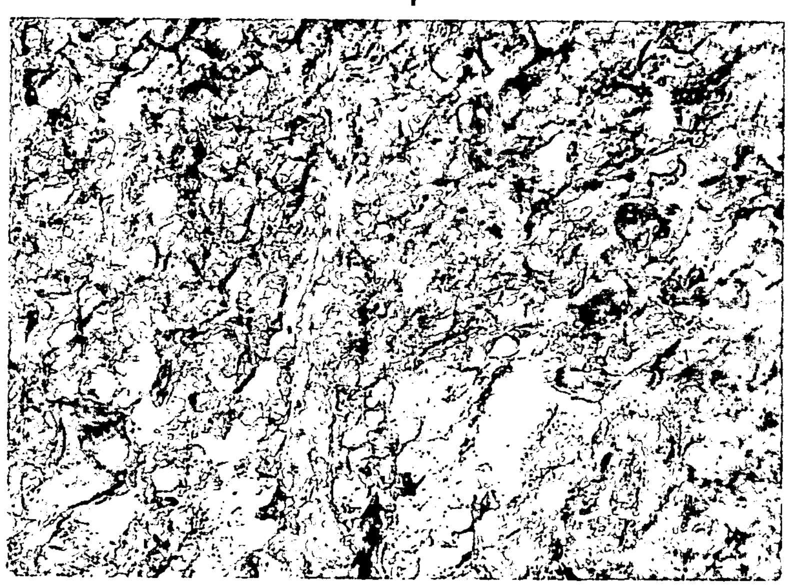


FIG. 11B

Mouse Zmax1 In situ hybridization
400X Magnification
Antisense probe

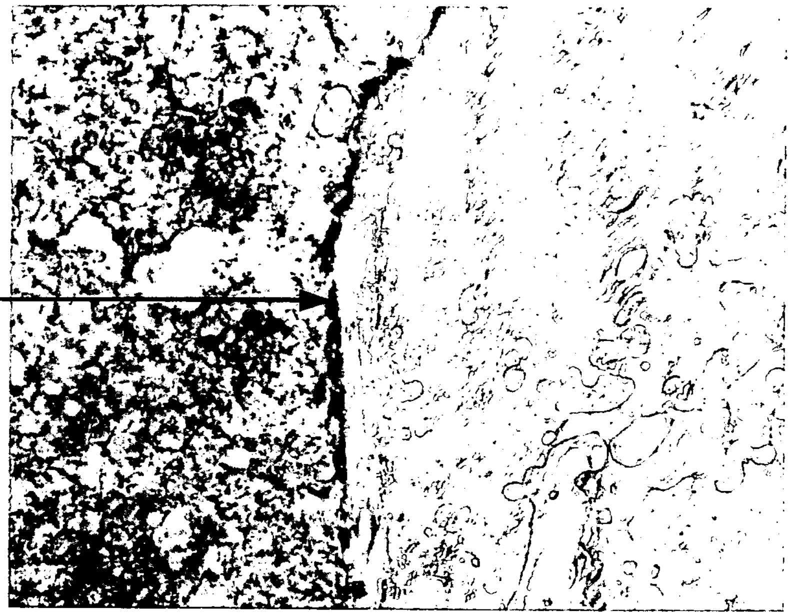



FIG. 12A

Mouse Zmax1 In situ hybridization
400X Magnification
Sense probe

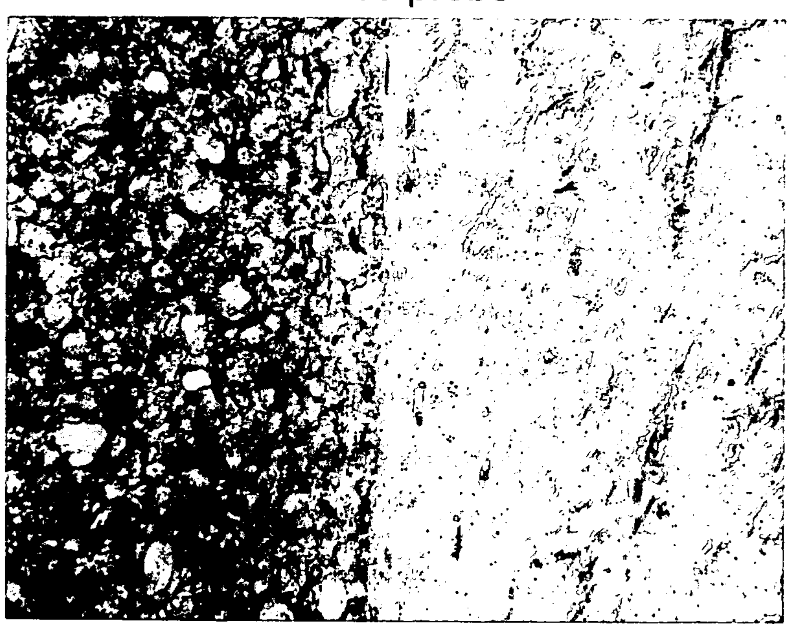
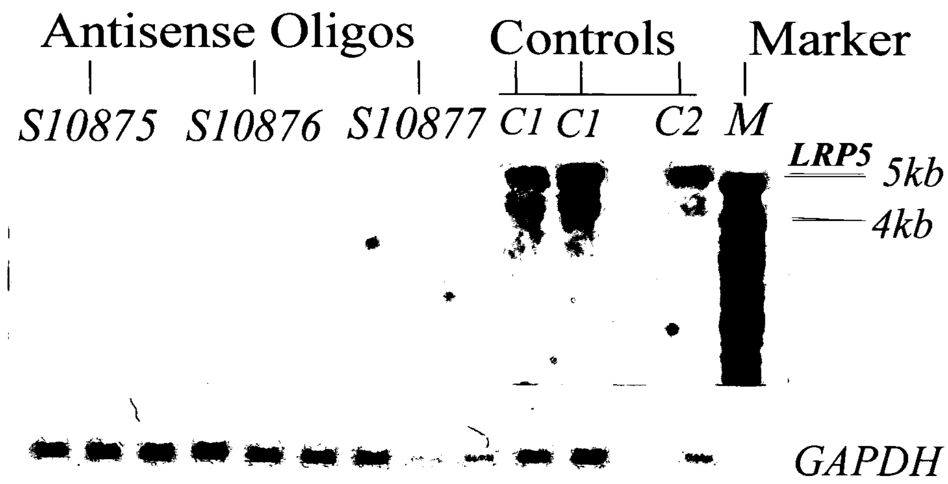


FIG. 12B

Antisense Inhibition of Zmax1 Expression




MC-3T3 cells

FIG. 13